

claims 60-67 can be found at page 24, line 23 through page 25, line 5. New claims 45-68 are considered to be consistent with the elected invention, as they are drawn to SVPH1 polypeptides of Groups XII-XXIV. The Examiner is respectfully requested to note that claims 46, 52, 59, and 68 recite further combinations of the subcombinations recited in the claims from which they depend, and therefore inclusion of these claims within Groups XII-XXIV is proper.

Attached hereto is Appendix A, captioned "Marked-Up Version to Show Changes Made", which shows the amendments made to the title and claims using standard notation (underlining and bracketing). Appendix B presents the pending claims in rewritten form. Applicant respectfully requests reconsideration and allowance of the claims pending.

**REJECTION UNDER 35 U.S.C. §101 and §112, First Paragraph**

Claims 4-6 and 13 were rejected under 35 U.S.C. §101 and §112, first paragraph, on the basis that these claims allegedly lack patentable utility, and that one skilled in the art would therefore not know how to use the invention. For the following reasons, these rejections have been overcome.

The arguments of the Office Action are addressed to the utility of SVPH1 metalloproteases. Applicant does not accede to this basis for the rejections, because the U.S. Patent Office has recently issued patents such as U.S. Patent No. 6,485,956, which has claims to SVPH family polypeptides having proteinase activity. Furthermore, the basis for the rejections as stated in the Office Action does not apply to claims 4-6 and 13 as amended, and the newly added claims, because they are drawn to polypeptides having *disintegrin* activity and comprising the *disintegrin* domain of the SVPH1 polypeptides and active variants thereof. The patentable utility of disintegrin polypeptides has also been recognized by the U.S. Patent Office, which has recently issued patents such as U.S. Patent No. 6,485,956 which also has claims drawn to SVPH family polypeptides having disintegrin activity. For at least these reasons, the claims as presented are considered to have a utility that is credible, specific, and substantial.

Withdrawal of the rejections of claims 4-6 and 13 under 35 U.S.C. §101 and §112, first paragraph is respectfully requested.

Should the Examiner have any questions, or believes that a teleconference would be

The Examiner is authorized to charge any required fees or credit any overpayments to Deposit Account Number 09-0089.

Respectfully submitted,



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IN THE TITLE:

**Appendix A**  
**U.S. Serial No. 09/890,323**  
**Marked-Up Version to Show Changes Made**

The Title has been amended as follows:

METALLOPROTEINASE-DISINTEGRIN [FAMILY MEMBERS: SVPH DNAS AND]  
POLYPEPTIDES

**IN THE CLAIMS:**

Claims 4 and 13 have been amended as follows:

4 (amended). An isolated polypeptide having disintegrin activity encoded by [the]a nucleic acid molecule [of claim 1] selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising a DNA sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9;

(b) an isolated nucleic acid molecule encoding an amino acid sequence comprising the sequence selected from the group consisting of amino acids 389 through 491 of SEQ ID NO:12, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14;

(c) an isolated nucleic acid molecule that encodes a polypeptide having disintegrin activity and that hybridizes to either strand of a denatured, double-stranded DNA comprising a nucleic acid sequence of (a) under hybridization conditions of 50% formamide and 6XSSC, at 42°C with washing conditions of 68°C, 0.2X SSC, 0.1% SDS; and

(d) an isolated nucleic acid molecule degenerate from SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9 as a result of the genetic code.

13 (amended). An isolated [metalloproteinase-]disintegrin polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, and [amino acids 1 through 15 of SEQ ID NO:12, amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, [amino acids 389 through 491 of SEQ ID NO:12], amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID

**Appendix B**  
**U.S. Serial No. 09/890,323**  
**Pending Claims as Presented December 2002**

Claims 1-3, 7-12, and 14-44: Canceled.

Claims 4 and 13: Amended.

Claims 45-68: Added

4 (amended). An isolated polypeptide having disintegrin activity encoded by a nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising a DNA sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9,

(b) an isolated nucleic acid molecule encoding an amino acid sequence comprising the sequence selected from the group consisting of amino acids 389 through 491 of SEQ ID NO:12, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14;

(c) an isolated nucleic acid molecule that encodes a polypeptide having disintegrin activity and that hybridizes to either strand of a denatured, double-stranded DNA comprising a nucleic acid sequence of (a) under hybridization conditions of 50% formamide and 6XSSC, at 42°C with washing conditions of 68°C, 0.2X SSC, 0.1% SDS; and

(d) an isolated nucleic acid molecule degenerate from SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9 as a result of the genetic code.

5. An isolated polypeptide according to claim 4 having a molecular weight selected from the group consisting of approximately 86,983; 89,459; and 92,781 Daltons as determined by SDS-PAGE.

6. An isolated polypeptide according to claim 4 in non-glycosylated form.

13 (amended). An isolated disintegrin polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, and amino acids 389 through 491 of SEQ ID NO:12

selected from the group consisting of amino acids 1 through 15 of SEQ ID NO:12, amino acids 16

through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14.

46 (NEW). The isolated polypeptide of claim 4 further comprising the amino acid sequence of a polypeptide selected from the group consisting of a poly-His peptide, a FLAG peptide, a peptide linker, a leucine zipper domain, and an Fc polypeptide.

47 (NEW). The isolated polypeptide of claim 4 comprising amino acids 389 through 491 of SEQ ID NO:12.

48 (NEW). The isolated polypeptide of claim 4 comprising SEQ ID NO:12.

49 (NEW). The isolated polypeptide of claim 4 comprising SEQ ID NO:13.

50 (NEW). The isolated polypeptide of claim 4 comprising SEQ ID NO:14.

51 (NEW). The isolated disintegrin polypeptide of claim 13 comprising amino acids 389 through 491 of SEQ ID NO:12 and further comprising an amino acid sequence selected from the group consisting of amino acids 1 through 15 of SEQ ID NO:12, amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14.

52 (NEW). The isolated disintegrin polypeptide of claim 13 further comprising the amino acid sequence of a polypeptide selected from the group consisting of a poly-His peptide, a FLAG peptide, a peptide linker, a leucine zipper domain, and an Fc polypeptide.

comprising said recombinant nucleic acid under conditions promoting expression of the

polypeptide, and wherein said recombinant nucleic acid comprises a nucleotide sequence encoding the polypeptide and selected from the group consisting of:

- (a) SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9;
- (b) a nucleotide sequence encoding an amino acid sequence comprising a sequence selected from the group consisting of amino acids 389 through 491 of SEQ ID NO:12, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14;
- (c) a nucleotide sequence that encodes a polypeptide having disintegrin activity and that hybridizes to either strand of a denatured, double-stranded DNA comprising a nucleotide sequence of (a) under hybridization conditions of 50% formamide and 6XSSC, at 42°C with washing conditions of 68°C, 0.2X SSC, 0.1% SDS; and
- (d) a nucleotide sequence degenerate from SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9 as a result of the genetic code.

54 (NEW). The polypeptide of claim 53, wherein the polypeptide is expressed by a method further comprising purifying the expressed polypeptide.

55 (NEW). The polypeptide of claim 53, wherein the polypeptide is expressed by a method comprising culturing a host cell selected from the group consisting of bacterial cells, yeast cells, plant cells, and animal cells.

56 (NEW). The polypeptide of claim 55, wherein the polypeptide is expressed by a method comprising culturing a mammalian host cell.

57 (NEW). The polypeptide of claim 53 having a molecular weight selected from the group consisting of approximately 86,983; 89,459; and 92,781 Daltons as determined by SDS-PAGE.

58 (NEW). The polypeptide of claim 53 in non-glycosylated form.

59 (NEW). The polypeptide of claim 53, wherein the polypeptide further comprises the amino acid sequence of a polypeptide selected from the group consisting of a poly His peptide, a FLAG

60 (NEW). An isolated polypeptide having disintegrin activity and having at least 80% amino acid identity with at least 30 contiguous amino acids of amino acids 389 through 491 of SEQ ID NO:12.

61 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide has at least 90% amino acid identity with at least 30 contiguous amino acids of amino acids 389 through 491 of SEQ ID NO:12.

62 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide has at least 95% amino acid identity with at least 30 contiguous amino acids of amino acids 389 through 491 of SEQ ID NO:12.

63 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide has at least 98% amino acid identity with at least 30 contiguous amino acids of amino acids 389 through 491 of SEQ ID NO:12.

64 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide comprises at least 20 contiguous amino acids of amino acids 389 through 491 of SEQ ID NO:12.

65 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide comprises at least 30 contiguous amino acids of amino acids 389 through 491 of SEQ ID NO:12.

66 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide further comprises an amino acid sequence selected from the group consisting of amino acids 1 through 15 of SEQ ID NO:12, amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14.

67 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide further comprises an

amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12,

amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14.

68 (NEW). The isolated polypeptide of claim 60, wherein the polypeptide further comprises the amino acid sequence of a polypeptide selected from the group consisting of a poly-His peptide, a FLAG peptide, a peptide linker, a leucine zipper domain, and an Fc polypeptide.